PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44*bis*)

Applicant's or agent's file reference FNI/CLY/060111	**FOR FURTHER ACTION**	See item 4 below
International application No. PCT/EP2006/003974	International filing date *(day/month/year)* 07 April 2006 (07.04.2006)	Priority date *(day/month/year)* 08 April 2005 (08.04.2005)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant LABORATOIRES BESINS INTERNATIONAL		

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 *bis*.1(a).

2. This REPORT consists of a total of 7 sheets, including this cover sheet.

   In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

☒	Box No. I	Basis of the report
☐	Box No. II	Priority
☐	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
☐	Box No. IV	Lack of unity of invention
☒	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
☐	Box No. VI	Certain documents cited
☐	Box No. VII	Certain defects in the international application
☐	Box No. VIII	Certain observations on the international application

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44*bis*.3(c) and 93*bis*.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44*bis* .2).

	Date of issuance of this report 09 October 2007 (09.10.2007)
The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No. +41 22 338 82 70	Authorized officer Yolaine Cussac e-mail: pt11.pct@wipo.int

Form PCT/IB/373 (January 2004)

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)* see form PCT/ISA/210 (second sheet)	
Applicant's or agent's file reference see form PCT/ISA/220	**FOR FURTHER ACTION** See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2006/003974	07.04.2006	08.04.2005

International Patent Classification (IPC) or both national classification and IPC
INV. A61K47/10 A61K47/12 A61K31/565 A61P5/50

Applicant
LABORATOIRES BESINS INTERNATIONAL

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:	Date of completion of this opinion	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	see form PCT/ISA/210	Schüle, S Telephone No. +31 70 340-4865

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

      ☐ a sequence listing

      ☐ table(s) related to the sequence listing

   b. format of material:

      ☐ on paper

      ☐ in electronic form

   c. time of filing/furnishing:

      ☐ contained in the international application as filed.

      ☐ filed together with the international application in electronic form.

      ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-17
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-17
Industrial applicability (IA)	Yes:	Claims	1-17
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item III.

The term "steroid in the testosterone synthetic pathway " is unclear and moreover relates to an extremely large number of possible substances. It is not obvious which steroids result from the testosterone synthetic pathway. This would require an equally unquantifiable and thus unreasonable amount of experimentation, imposing a severe and undue burden on all those wishing to ascertain the scope of the claim, which is not in compliance with the clarity requirement of Article 6 PCT. The non-compliance with the substantive provisions is to such an extent, that the search was performed taking into consideration the non-compliance in determining the extent of the search (PCT Guidelines, 9.19 and 9.24).

The extent of the search was consequently limited to the clearly defined active ingredients disclosed in the application, in fact to

androisoxazole, androstenedione, bolasterone, clostebol, ethylestrenol, formyldienolone, 4-hyclroxy-19-nortestosterone, methenolone, methyltrienolone, nandrolone, oxymesterone, quinbolone, stenbolone, trenbolone, boldenone, dehydroepiandrosterone, fluoxymesterone, mestanolone, mesterolone, methandrostenolone, 17-alpha- methyltestosterone, 17-alpha-methyl-testosterone 3-cyclopentyl enolether, norethandrolone, normethandrone, oxandrolone, oxyrnetholone, prasterone, stanlolone, stanozolol, dihydrotestosterone, testosterone, anagestone, chlormadinone acetate, delmadinone acetate, demegestone, dimethisterone, dihydrogesterone, ethinylestrenol, ethisterone, ethynodiol, ethynodiol diacetate, flurogestone acetate, gestodene, gestonorone caproate, haloprogesterone, 17-hydroxy-16-methylene-progesterone, 17-alpha-hydroxyprogesterone, 17-alpha-hydroxyprogesterone caproate, medrogestone, medroxyprogesterone, megestrol acetate, melengestrol, norethindrone, norethindrone acetate, norethynodrel, norgesterone, norgestimate, norgestrel, norgestrienone,19-norprogesterone, norvinisterone, pentagestrone, prenenolone, progesterone, promegestone, quingestrone, and trengestone

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Documents

Reference is made to the following documents

D1: US 2003/022877 A1 (DUDLEY ROBERT E) 30 January 2003 (2003-01-30) cited in the application

D2: MÜLLER ET AL.: "Testosterontherapie des Hypogonadismus" SCHWEIZERISCHE ÄRZTEZEITUNG, vol. 81, no. 46, 2000, pages 2589-2593, XP002389108

2. Independent Claim 1

2.1 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of **claim 1** does not involve an inventive step in the sense of Article 33(3) PCT.

2.2 The document D1 is regarded as being the closest prior art to the subject-matter of claim 1 and discloses a composition comprising 0.1 - 10% testosterone, 30 - 98% alcohol selected from the group consisting of ethanol and isopropanol, 0.1 - 5% isopropylmyristate, 1 - 5% sodium hydroxide, and 0.1 - 5% of a gelling agent (claim 1). The hydroalcoholic gel is applied for the treatment of testosterone deficient disorders such as hypogonadism, sexual dysfunction, hyperglycemia, hyperinsulinemia, hypoinsulinemia which are listed on p. 8, paragraph 81.

2.3 The subject-matter of **claim 1** therefore differs from this known in that the composition is applied for the treatment and/or prevention of diabetes.

2.4 The problem to be solved by the present invention may therefore be regarded as providing a formulation for the treatment of diabetes.

2.5 The solution proposed in **claim 1** of the present application cannot be considered as involving an inventive step (Article 33(3) PCT), because D1 already discloses the composition of the claimed hydroalcoholic gel and mentions that hyperglycemia and

hypoinsulinemia are among the diseases which are treated by application of the testosterone comprising gel. This already indicates that the gel might be used for the treatment of diabetes. D2 discloses that the application of testosterone increases the insulin sensitivity, so that testosterone application is recommended for the treatment of diabetes typ -2. Furthermore, the document indicates that diabetes mellitus is often associated with a testosterone deficiency and provides a link to D1. Therefore, it would have been obvious for the person skilled in the art to combine the teachings of the two documents. Moreover, the application does not give any evidence that diabetes can be treated with testosterone, it merely describes the implementation of a clinical trial without providing results. Therefore, the problem is not solved and the subject-matter of claim 1 does not involve an inventive step.

2.6 Dependent **claims 2 - 17** do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, because the subject-matter of these claims is already disclosed in D1.

3. **INDUSTRIAL APPLICABILITY** (Art. 33(4) PCT)

3.1 The subject-matter of **claims 1 - 17** is industrial applicable according to Art. 33(4) PCT.